Endothelial cells from embryonic stem cells in a chemically defined medium.

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Public Summary:
Endothelial cells (ECs) are desired for their therapeutic potential in a variety of areas including gene therapy, cardiac regeneration, development of tissue-engineered vascular grafts, and prevascularized tissue transplants. Pluripotent embryonic stem cells (ESCs) can be induced to differentiate into ECs in vitro using embryoid bodies, monolayer cultures, or by genetic manipulation and immortalization. However, obtaining homogeneous cultures of proliferating ESC-derived ECs without genetic manipulation is a challenging undertaking and often requires optimization of protocols and rigorous purification techniques. Moreover, current differentiation methods that use medium containing fetal calf or bovine serum components introduce additional challenges because of our limited ability to control the differentiation signals and batch-to-batch variations of serum. We have explored the development of new medium formulations for deriving ECs from murine embryonic stem cells (mESCs) using only chemically defined reagents. We present 2 different medium formulations along with the detailed methodologies, including the optimization of extracellular matrix-derived substrates known to play a role in cell attachment and proliferation as well as cell differentiation.

Scientific Abstract:
Endothelial cells (ECs) are desired for their therapeutic potential in a variety of areas including gene therapy, cardiac regeneration, development of tissue-engineered vascular grafts, and prevascularized tissue transplants. Pluripotent embryonic stem cells (ESCs) can be induced to differentiate into ECs in vitro using embryoid bodies, monolayer cultures, or by genetic manipulation and immortalization. However, obtaining homogeneous cultures of proliferating ESC-derived ECs without genetic manipulation is a challenging undertaking and often requires optimization of protocols and rigorous purification techniques. Moreover, current differentiation methods that use medium containing fetal calf or bovine serum components introduce additional challenges because of our limited ability to control the differentiation signals and batch-to-batch variations of serum. We have explored the development of new medium formulations for deriving ECs from murine embryonic stem cells (mESCs) using only chemically defined reagents. We present 2 different medium formulations along with the detailed methodologies, including the optimization of extracellular matrix-derived substrates known to play a role in cell attachment and proliferation as well as cell differentiation. Characterization of the ESC-derived ECs indicate that (1) chemically defined medium formulations reproducibly generate superior ECs compared with previous serum-containing formulations, (2) fibronectin, and not collagen type-IV, is the optimal substrate for EC induction in our chemically defined medium formulations, (3) without additional activation of Notch-signaling, ESC-ECs develop predominantly into venous ECs, and (4) using these medium formulations, a second rigorous selection step is not required to generate proliferating ECs from ESCs, but it does enhance the final purity of the ECs.